

## The Editors Desk

**Ever wonder why chirality has been ignored for so many years, even though the brightest scientists in the past 100 years----including Pasteur and Einstein---knew that, for the sake of mankind, it could NOT be ignored?**

**Until recently, pharmaceutical companies went out of their way to ignore chirality. Now they are falling all over themselves (and spending many billions of dollars in the process) to offer "chirally-correct" drugs. Why the delay?**

Please read on, as one of SuperNatural's core product developers answers this nagging question by looking into the mind of one man. Here is their response . . .

### THE ANATOMY OF DANGEROUS IGNORANCE

. . . You might ask yourself: what kind of person would minimize the importance of chirality? What kind of person would label concern about chirality a "chiral trap".

Remember in the 1950s and early 1960s, there was this drug called THALIDOMIDE. How many people suffered monstrous deformities and slow death because the pharmaceutical company that manufactured it didn't believe in the relevance of "chiral-correctness" to thalidomide's activity? Women were given the chirally-incorrect mixture of left and right-handed molecules. The left-hand was the bad, chirally-incorrect molecule (which caused gross deformities in the fetus). It's mirror-image was the good, chirally-correct molecule (which had the sedative effect).

Or how about the anti-hyperactivity drug RITALIN? How much damage has been caused by this drug which has for years been marketed to children as a toxic brew of both left and right-handed molecules??? It is the right-handed methylphenidate that gives Ritalin its benefits, while the left-handed molecule contributes nothing but unhealthy side-effects. We coined the term "chirally-correct" to denote the healthy molecule, and "chirally-incorrect" to denote its unhealthy mirror-image or evil twin.

Why have the pharmaceutical companies been KNOWINGLY marketing a chirally-incorrect drug to children? We asked them this, and they said that we were making too big a deal about chirality. The original drug company to market thalidomide denied the existence of "chiral correctness" to the detriment of millions of women and their doomed children.

Can such ignorance exist today?

Only in the steamy, fetid backwaters of the inbred skin care industry.

Fast forward to a glossy trade magazine called "Skin Inc". A recent article by Peter Pugliese "MD" will give us a glimpse into a mind that harkens back to a time when dangerous ignorance roamed the pharmaceutical industry like a T-Rex on dexadrine, killing and maiming millions.

Now, remember that real skin care nibbles around at the edges of medicine itself. If you take this business seriously, you must be aware that the skin is an important organ of the body. And doing serious skin care entails the treatment of skin problems (not just age-related) on some level.

In fact, the most serious-minded in this business constantly (but respectfully) flirt with the regulatorily-drawn lines between cosmetics and medicine. Presumably, anyone in this business with an "MD" after their name would be the most cognizant of the potential importance----and therefore responsibility----of actions by formulators in "pushing the envelope" when seriously addressing skin problems.

Now, bear in mind, the first company in skin care to introduce the concept of "chirality" was (omitted to protect our supplier). It was our company (omitted to protect our supplier) that coined the term "chirally-correct".

One would think that a "medical doctor" who constantly surveys the cosmetic landscape for encouraging signs of emerging substance would use his medical knowledge to encourage interest in chirality----which the pharmaceutical industry is now determining to be the most critical issue in health care today. Isn't skin care a part of health care? Ask the aestheticians who read Skin Inc!

Here is "Dr." Pugliesi's response to the introduction of chirality into the health care of the skin...

*"More and more often, it's being asked if a product's chirality is correct. What should be asked is if the product is biologically active."*

This was exactly the benchmark used in qualifying hundreds of drugs for the market-place (over just the past 50 years)----drugs which did far more harm than good because of ignoring the obvious question: is our product's chirality correct. The offending pharmaceutical company asked only if it was biologically active.

*"Most chemical compounds in nature are chiral compounds and are correct chirally."*

So, "doc", you believe that all chiral compounds in nature are "correct chirally"? Now, don't forget, we're talking about the human body. You're blabbing away in SKIN Inc, not Better Homes and Gardens! We don't mean chirally-correct for the plant----it's obvious that it is! But is this kind of chiral-correctness equally applicable to the skin (or any other part of the body)? Most biological molecules are, as you mentioned, chiral. But most biological molecules can be found in either hand----if you look hard enough (sometimes even in the same plant). An easy example is turpentine, which comes from noble fir cone. Turpentine contains both L-LIMONENE and D-LIMONENE. It is a truism in stereochemistry that the two opposite hands (enantiomers or chirons) of a molecule do not and CAN NOT have the same chemical activity. This means quite simply that if one hand is correct (which is determined by its chemical activity in a specific physiological venue), the other MUST BE INCORRECT (relative to the same venue)!!! Your statement above says that L-LIMONENE and D-LIMONENE are equally chirally-correct (they are in

fact NOT, as any perusal of the medical literature will reveal!). This is precisely the position taken by pharmaceutical companies during America's medical "Dark Ages" (10 to 50 years ago). We assure you that if there is different biological activity between these two chirons (hands)----and there is!----one will be better for you than the other (or one will not be as bad for you as the other).

*"Asking if it is 'chirally correct' is the same as asking 'Is the water in this product really H<sub>2</sub>O?' There is no such thing as chirally correct, any more than you can be facially correct. What should be asked is, 'Does this product have the correct optical isomerism?' By being correct it is biologically active."*

How can this "medical doctor" know what is meant by "chirally correct" when we are the sole originators of the term? He is telling us what we mean by our own terminology. He did not call us or write to us and ask us what we meant by the term (which would be odd anyway, since to all the other doctors it is perfectly self-explanatory in the venue with which they are most familiar----pharmaceutics!). He had to know that this was our term (i.e. a term used by us and our 'disciples', the companies that learn from us). A simple sojourn through the World Wide Web on your favorite search engine (try Google or HotBot in the "advanced" search mode) and see the few sites containing "chirally-correct". Notice the uniformity of useage? This is an indication that there is only one accepted use of the term. So, why did "Doctor" Pugliesi recklessly pick the most bizarre, twisted interpretation imaginable for a "medical doctor"? You would expect one the general readership of mainstream cosmetics journals to make such an error in judgment, not the "doc" who makes a living talking down to them in barely decipherable medico-babble.

Can you imagine teaching people----most of whom have never had a chemistry course----that asking if a product has the "correct optical isomerism" is more meaningful than asking if it has correct chirality (which the "doc" considers to be as ludicrous as asking if the water in your product is really H<sub>2</sub>O)? Why should we make an already difficult concept immensely more difficult by simply substituting the word "chirality" with "optical isomerism"? Have mercy on these people, "doc". Chirality is new to skin care, so help them understand it better. These are the same ladies who suffer disproportionately more than men at the hands of the health system you perpetuate just because they make the cost of appropriately representative clinical trials soar and they tend to be more dependent on the chirally-incorrect pharmaceutical companies (with the well-intentioned encouragement of the often chirally-ignorant doctors) because their body chemistry is vastly more sensitive than a man's.

And you say that being chirally-correct, a molecule is simply biologically active and nothing more? So, by being chirally-incorrect, it is not biologically active? Tell that to the victims of all those teratogenic pharmaceuticals given innocent expectant mothers during the better part of the last century. These were ALL chiral compounds. And they were all "racemic" (i.e. equal portions of left and right handed or mirror image molecules). So the bad mirror image (i.e. the wrong-handed molecule) is not biologically active??? Take your speech to the next international

conference of chiral chemistry and see how much effort and imagination is required to mistake the attendees reaction as being applause...

*"There are a few other words that should be understood to appreciate the full significance of the chiral trap."*

He goes on to talk about isomers and epimers and enantiomers----just textbook stereochemistry. But he piles on the very words and ideas that can only serve to alienate ordinary people from the most important technical concept in their lives. I've used the word "enantiomer" a few times in my writings (peruse the website), but only after writing extensively about chirality in the more simple terms of "handedness". Why go beyond this? Why does one ever have to mention epimers and isomers, especially when these are not purely chiral concepts? They are stereochemical concepts that apply to a broad category of compounds, only some of which are chiral. So why use a broader concept to describe a very narrow concept, and then criticize people who bend over backward to make the chiral concept palatable to the non-technical aesthetician who conscientiously reads Skin Inc. and other journals as a means of self-education?

And why go even farther out on this quivering limb to call what these chiral neophytes are doing as being "the chiral trap"? Are you saying that what these people (the marketers of chiral products) are doing is alot of bunk? Are you saying that chirality's application to any aspect of health care is bunk? Are you saying that even though chirality has legitimacy in medicine, it is nothing to get excited about in skin care? Are you saying that it is a trap for people to respond favorably to the introduction of chirality into their awareness of themselves and the world around them? Are you saying that it is a trap for people to buy chiral skin care products from me or my clients or colleagues, but not from you and your organization or anyone else unless they use the words "isomer" and "epimer" and "enantiomer"?

Oh, I see. You may think that since ingredient labels of 'new-age' chiral products show D-GLUCOSE or L-PROLINE that this is just a word game in an attempt to elevate an ordinary skin care product containing ordinary sugar and ordinary protein to something special, thereby giving it an unfair advantage over the other 'honest' cosmetic hucksters. This would be a fair suspicion if it weren't for these facts:

1. There are usually other not-so-obvious chiral ingredients on the label (with a long pharmaceutic history) like L-MENTHOL instead of D-MENTHOL or DL-MENTHOL, or D-ALPHA-TOCOPHEROL instead of L-ALPHA-TOCOPHEROL or DL-TOCOPHEROL, or L-LIMONENE instead of D-LIMONENE or DL-LIMONENE, etc. So there are responsible, educated choices that can be made. It's not a con word-game like you suggest!
2. Synthetic ingredients are usually racemic when they come to market, this explains the DL or dl prefix to a number of popular nutrients used both internally and topically. Using a chiral prefix denoting handedness is a

helpful way to determine if an ingredient is synthetic or natural (like Vitamin-E).

3. Using chiral prefixes for common sugars and amino acids that come in only one optical "flavor" or orientation anyway is the BEST way to make people---who have never heard of optical activity or chirality or left-hand-right-hand or mirror image molecules (let alone isomer, epimer, enantiomer)----AWARE of how close they have been to chiral reality all their life, and how important it is to Life itself. My question here is HOW CAN YOU NOT put a "D" in front of your sugars and an "L" in front of your amino acids????????? If you are going to educate people on chirality, and implement a label protocol that dovetails with this nicely, it would be even more questionable to NOT do this.

Finally, you wrap up your "Notes on chirality" article with these words:

*"In some cases, a dl-form of a vitamin can be found on an ingredient label. In that case, one of the forms is inactive. At times it is less expensive to use twice as much of a racemic form of a material than to use the pure d- or l-form."*

So, your whole 'thesis' seems to be that chirality is inconsequential to skin care because skin care is confined to non-interesting chiral compounds that have only one biologically-active hand (D-sugars and L-amino acids), while the other hand is non-threatening because it is inactive. The only latitude a formulator has----according to you----is to 'doctor' the label to make the ingredients appear to be chirally interesting, when in fact they are not.

Looking at the history of the pharmaceutical industry, it is interesting how this rationale evolved with the revolution in synthetic chemistry that gave us a long list of racemic drugs derived from petroleum, supplanting the chirally-pure extracts (i.e. one hand or enantiomer, instead of the other or both) made available by natural-products chemistry earlier.

It is also very interesting, dear "doctor", that you acknowledge the viability of the economics argument that it's cheaper and easier to give people the synthetic racemate (mixture of left and right) than to separate the biologically "correct" (or "active", as you put it) hand from the biologically-incorrect hand. I say "interesting" because:

1. You're a "doctor", and
2. This is PRECISELY the argument used by the pharmaceutical industry this past century to keep from investigating the dubious tenet that chiral molecules come in only two 'flavors': active and inactive.

For those of you (like myself) who have wondered how the BIGGEST SCANDAL in the history of societally-administered health (which could rate as being the biggest scandal of all time, considering the lives involved at the hands of a group that supposedly has a vested interest in preserving life) could escape public scrutiny for so long, we now have a glimpse of the kind of self-serving cynicism that congealed

under its own well-healed weight into a mass-effort to keep us at-all-costs ignorant (and increasingly dependent on the health-care system).

"Doc", you've been caught in the act of being your own (and our) worst enemy, but making it look like you are just doing your job and trying to help people. You're a real 'pro'.

In a word, gotcha!